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EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,651	SCHOR ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2002 and 08 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,27,29,36-42,44,47-51,53 and 56-59* is/are pending in the application.

4a) Of the above claim(s) *36-42,44,47-51,53 and 58* is/are withdrawn from consideration.

5)☒ Claim(s) *4 and 5* is/are allowed.

6)☒ Claim(s) *1-3, 6-13,27,29,56,57 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 July 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20020326*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The election filed August 15, 2002 is acknowledged and has been entered. Applicant has elected the invention of Group I, claims 1-13, 27, 29, 51, 56, 57, and 59, drawn to a nucleic acid molecule encoding a polypeptide, a vector comprising said nucleic acid molecule, a host cell comprising said vector, a polypeptide encoded by said nucleic acid molecule, a method for producing said polypeptide, an agent comprising said polypeptide, and a pharmaceutical composition comprising said polypeptide.

Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. The supplemental election filed March 8, 2004 is acknowledged and has been entered. Applicant has elected the species of the invention of Group I, wherein the peptide of claim 27 and 29 is a peptide comprising the amino acid sequence of SEQ ID NO: 3.

Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. The amendment filed March 8, 2004 is acknowledged and has been entered in part; see the response to the amendment set forth below. Claims 14-26, 28, 30-35, 43, 45, 46, 52, 54, and 55 have been canceled. Claims 27, 37-42, and 51 have been amended.

4. Claims 1-13, 27, 29, 36-42, 44, 47-51, 53, and 56-59 are pending in the application. Claims 36-42, 44, 47-51, 53, and 58 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

With regard to claim 51, as amended on July 30, 2004, the claim is drawn to a method for modulating cell migration at a site within a mammalian body comprising administering to the site a polypeptide according to any one of claims 10 and 12; whereas previously claim 51 was drawn to the use of a polypeptide in the manufacture of an agent for modulating cell migration. PCT Rules 13.1 and 13.2 do not provide for a single general inventive concept comprising more than the first claimed product, more than the first claimed method for producing said product, or more than the first claimed method for using said product. Accordingly, claim 51 has been withdrawn from further consideration as being drawn to a nonelected invention.

Since the examiner has restricted product and process claims and Applicant has elected claims directed to the product, it is noted that once a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain

dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

5. Claims 1-13, 27, 29, 56, 57, and 59 are currently under prosecution.

Information Disclosure Statement

6. The information disclosure filed March 18, 2002 has been considered. An initialed copy is enclosed.

Response to Amendment

7. The substitute specification filed July 30, 2004 is acknowledged but has not been entered, because the marked-up copy of the substitute specification fails to show each and every change made relative to the immediate prior version of the specification. See MPEP § 608.01(q) [R-2]. See 37 CFR § 1.125.

In this instance, it appears that the changes already made to the originally filed specification by the amendment filed November 6, 2003 were not considered during the preparation of the substitute specification. As such, the marked-up copy of the substitute specification fails to show the deletion of the paragraph at page 1, which was added by the amendment filed November 6, 2003. Furthermore, the marked-up copy fails to show the deletion of "SEQ ID NO: 43" and its replacement by the insertion of "SEQ ID NO: 12"; however, the sequence disclosed at page 24 in line 38 is properly identified as SEQ ID NO: 43, not SEQ ID NO: 12, and therefore it is noted that the change made in the substitute specification would undo the proper change made previously by the amendment filed November 6, 2003.

Drawings

8. The drawing sheet setting forth Figure 2 (Part 2) is objected to because "SEQ ID NO." is misspelled as "SEQ IS NO." in both instances. Appropriate correction is required.

Specification

9. The abstract filed July 30, 2004 is objected to because it consists of more than one paragraph. See MPEP § 608.01(b) [R-2].

10. The disclosure is objected to for the following reason: The specification contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). Sequences appearing in the specification and/or drawings must be identified by sequence identifier in accordance with 37 C.F.R. 1.821(d). According to 37 CFR § 1.821(a), an unbranched sequence of four or more specifically identified amino acids or an unbranched sequence of ten or more nucleotides must be identified by sequence identification numbers. See MPEP § 2422.01.

Noting that the substitute specification filed July 30, 2004 has not been entered, as explained above, the instant specification, as originally filed June 15, 2000 and as since amended on November 3, 2003, is deficient. Because the substitute specification has not been entered, the changes that would have been made to correct these deficiencies have not been made. There are sequence disclosures, which are not properly identified at pages 4 and 5, page 5 (line 15), pages 6 and 7, page 19, pages 19 and 20, page 21, page 22, page 23 (lines 4-8), page 24, page 24 (lines 34-38), page 26 (line 6), pages 26 and 27, pages 27 and 28, page 29, page 30, page 32, page 33, pages 33 and 34, pages 35 and 36, page 36, page 37, pages 38 and 39, page 39, page 45 (line 17), and page 47 (lines 25-29).

Applicant must provide appropriate amendments to the instant specification inserting the required sequence identifiers.

As noted in the attached Notice to Comply, appropriate action correcting this deficiency is required. If necessary to correct the deficiency, Applicant must submit paper and computer-readable copies of a substitute sequence listing, together with a statement that the content of both copies are the same and, where applicable, include no new matter.

11. The specification is objected to because the use of improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

An example of an improperly demarcated trademark is Qiagen™ (page 48, line 21).

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

12. The specification is objected to because of the following informalities:

(a) "Streptavidin" is misspelled as "streptaridin" at page 35 (line 15); and

(b) "Lipofectamine" is misspelled as "lipfectamine" at page 50 (line 15).

Claim Objections

13. Claim 2 is objected to because the claim recites, "the amino acid sequence shown in Figure 2 labeled pMSF1α between positions 19 and 660 (SEQ ID NO: 36)". SEQ ID NO: 36 is 657 amino acids in length; but the amino acid sequence shown in Figure 2 between positions 19 and 660 (i.e., the amino acid sequence initiating with the

methionine at position 20 of the sequence depicted and ending with tyrosine at position 659) is only 640 amino acids in length. Therefore, the amino acid sequence shown in Figure 2 between positions 19 and 660 is not SEQ ID NO: 36. In addition, the sequence in Figure 2 is labeled "MSF-1α", not "pMSF1α". Appropriate correction is required.

14. Claim 27 is objected to because "SEQ ID NO: 44" is mistyped as "SEC ID NO: 44". Appropriate correction is required.

15. Claim 29 is objected to because the claim recites, "any one of the sequences [...] or [...] or [...] or [...] or [...]", which is improper Markush-type claim language. See MPEP § 2173.05(h).

This issue can remedied by amending claim 29 to recite, for example, "any one of the sequences selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 35, and SEQ ID NO: 7".

Claim Rejections - 35 USC § 101

16. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

17. Claim 8 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 8 is broadly interpreted to encompass a host cell, which is not isolated and which is comprised within an organism, including a human. Moreover, the claim encompasses a cell within a human body comprising a recombinant polynucleotide of claim 1.

Support for this broad interpretation of the claim is found throughout the specification. For example, at page 44, lines 10 and 11, the specification contemplates the use of gene therapy to administer the polypeptide. At page 42, lines 6-8, the specification teaches administering to a site within the human body.

MPEP § 2105 [R-1] states:

> If the broadest reasonable interpretation of the claimed invention as a whole encompasses a human being, then a rejection under 35 U.S.C. 101 must be made indicating that the claimed invention is directed to nonstatutory subject matter.

Amending claim 8 to recite "isolated" before "host cell" can obviate this ground of rejection.

Claim Rejections - 35 USC § 112

18. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

19. Claims 1-3, 6-13, 27, 29, 56, 57, and 59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, "Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

Claims 1-3, 6-13, 27, 29, 56, 57, and 59 are directed to a genus of nucleic acid molecules or of polypeptides, which each comprises members that vary markedly in both structure and function. For example, claim 1 is drawn to a genus of polynucleotides that encode a polypeptide that comprises SEQ ID NO: 1, a "variant" thereof, a "fragment" thereof, or a "derivative" thereof. The variants of SEQ ID NO: 1 vary in structure and do not necessarily have the same function as the polypeptide of SEQ ID NO: 1, so the polynucleotides encoding those variants vary in both structure

and function. Similarly, polypeptides comprising a mere fragment of SEQ ID NO: 1, or those merely derived from SEQ ID NO: 1 also vary substantially in structure; again, these polypeptides do not necessarily have the same function as the polypeptide of SEQ ID NO: 1, so the polynucleotides encoding the polypeptides comprising the fragments or derivatives of SEQ ID NO: 1 vary both in structure and function. Alternatively, the claims are directed to fusions of a polypeptide comprising a variant, fragment, or derivative of SEQ ID NO: 1; these fusions vary both in structure and function, just as the variants, fragments, or derivatives of which they are comprised.

In particular, it is noted that claim 12 is merely drawn to a polypeptide produced by a process comprising culturing the host cell of claim 8; accordingly, the claim is directed to any polypeptide produced by a host cell comprising a vector encoding a polypeptide according to claim 1. Therefore, the claim is directed to a genus of polypeptides having highly variable structures and functions, since a host cell produces an abundance of different proteins, which differ markedly in structure and function.

Claims 6, 13, and 59 recite a limitation that the polypeptide has "migration stimulation factor activity". However, the specification does not describe what functional activity or activities constitute "migration stimulation factor activity"; nor does the specification describe the methodology that can be used to identify, recognize, and distinguish such activity. Moreover, the specification does not appear to describe any one particularly identifying structural feature that is shared by at least a substantial number of the members of the genus of polypeptides that has this activity, so there does not appear to be a correlation between the recited functional attribute and a common structure feature. Accordingly, the skilled artisan could not immediately envision, recognize, or distinguish at least a substantial number of the members of the genus of polypeptides to which the claims are directed.

Were the "migration stimulation factor activity" adequately described, it is noted that in deciding *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the Court held that a generic statement that defines a genus of nucleic acids *by only their functional activity* does not provide an adequate written description of the genus. By analogy, a generic statement that defines the members of a genus of

polypeptides by only their common ability to function as a "migration stimulation factor" does not serve to adequately describe the genus as whole. The Court indicated that while applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a precise definition of a representative number of members of the genus, such as by reciting the structure, formula, chemical name, or physical properties of those members, rather than by merely reciting a wish for, or even a plan for obtaining a genus of molecules having a particular functional property. The recitation of a functional property alone, which must be shared by the members of the genus, is merely descriptive of what the members of genus must be capable of doing, not of the substance and structure of the members.

Claim 27 recites a limitation that the claimed molecule is capable of giving rise to antibodies that are reactive towards the polypeptide of SEQ ID NO: 1 following immunization of an animal with the molecule. Thus, the members of the claimed genus of molecules must share an antigenic determinant (epitope) that is recognized by an antibody that binds both to the molecule and the polypeptide. The presence of any given epitope on the polypeptide of SEQ ID NO: 1, however, is not correlated with any particularly identifying substantial structural or functional feature, so the claim is merely directed to a genus of polypeptides that are immunologically cross-reactive. The polypeptides vary markedly in both structure and function; and therefore the skilled artisan could not immediately envision, recognize, or distinguish at least a substantial number of the members of the genus of polypeptides to which the claims are directed.

Furthermore, claim 27 is directed to "natural variants" of the polypeptide of SEQ ID NO: 1. The claim is thus directed to a genus of polypeptides that encompasses naturally occurring proteins that have been synthesized recombinantly or chemically, as well as those isolated from nature, which comprise amino acid sequences that are variants of SEQ ID NO: 1. However, once a protein is made, it is not possible to determine how it was made; nor is it possible to determine its source. Thus, without a detailed written description of all of the naturally occurring variants of the polypeptide of SEQ ID NO: 1, the skilled artisan could not immediately envision, recognize, or

distinguish the natural variants of the polypeptide of SEQ ID NO: 1 from other polypeptides.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant had possession of the claimed invention at the time the application was filed.

The specification provides an adequate written description of the polypeptide of SEQ ID NO: 2, which is encoded by the polynucleotide sequence of SEQ ID NO: 1. Additionally, the specification adequately describes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 from the amino acid at position 20 (methionine) through the amino acid at position 659 (tyrosine), which is encoded by the polynucleotide sequence of SEQ ID NO: 1 from the nucleotide at position 57 to the nucleotide at

position 1982. Furthermore, the specification provides an adequate written description of a polypeptide consisting of SEQ ID NO: 3.

However, the description of these few members of the claimed genus of nucleic acid molecules is not sufficient to meet the requirements of 35 USC § 112, first paragraph, since the genus embraces widely variant members and an adequate description of such cannot be achieved by describing members, which are not representative of the genus. As disclosed and claimed, the genus of nucleic acid molecules does not comprise members having a common, particularly identifying structural feature that correlates with a common functional feature shared by at least a substantial number of its members. As such, absent any of the factual evidence of an actual reduction to practice discussed above, the skilled artisan could not immediately envision, recognize, or distinguish at least a substantial number of the members of the claimed genus said at least substantial number. Accordingly, the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

20. Claims 1-3, 6-13, 27, 29, 56, 57, and 59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using** a nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 1 from the nucleotide at position 57 through the nucleotide at position 1982, a replicable vector comprising said polynucleotide sequence, a host cell comprising said vector, a polypeptide, or composition thereof, comprising the amino acid sequence of SEQ ID NO: 1 from the amino acid at position 20 through the amino acid at position 659, a polypeptide consisting of the amino acid sequence of SEQ ID NO: 3, and a method for producing said polypeptide comprising culturing said host cell and isolating said polypeptide produced by the host cell, **does not reasonably provide enablement for making and using** a nucleic acid molecule encoding a polypeptide comprising a variant, fragment, or derivative of the amino acid sequence of SEQ ID NO: 1 or a nucleic acid molecule encoding a polypeptide comprising a fusion comprising said variant, fragment, or derivative, a replicable vector comprising said polynucleotide

sequence, a host cell comprising said vector, a polypeptide, or composition thereof, comprising an amino acid sequence of SEQ ID NO: 1 from the amino acid at position 20 through the amino acid at position 659, a polypeptide comprising of the amino acid sequence of SEQ ID NO: 3, or a method for producing said polypeptide comprising culturing said host cell and isolating said polypeptide produced by the host cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/or the invention commensurate in scope with these claims.

The amount of guidance, direction, and exemplification disclosed by Applicant would not be sufficient to enable the skilled artisan to make and/or use the claimed invention without a need to perform an undue amount of additional experimentation. Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The specification teaches a polypeptide designated MSF was described by the prior art; see, e.g., page 1, line 6. In addition, the specification teaches the polypeptide comprises the amino acid sequence set forth as SEQ ID NO: 1, which is encoded by a nucleic acid molecule comprising the polynucleotide sequence set forth as SEQ ID NO: 2; see, e.g., Figures 1 and 2.

The prior art teaches a 70 kDa polypeptide produced by fetal fibroblasts, which is designated MSF; see, e.g., Grey et al. (*Proc. Natl. Acad. Sci. USA*. 1989 Apr; **86**: 2438-2442) (of record). Grey et al. teaches the polypeptide stimulates the migration of fibroblasts that do not express the polypeptide into a collagen matrix; see, e.g., page 2439, column 1; and page 2441, Figure 1. The structure, mode of action, and possible function in health and disease is reviewed by Shor et al. (*Symp. Soc. Exp. Biol.* 1993; **47**: 235-251) (of record); see the entire document (e.g., the summary). In addition, Shor

et al. (Cell Motility Factors. 1991; 59: 127-146) (of record) teaches implications of the heterogeneity amongst fibroblasts in production of the polypeptide in cancer pathogenesis; see entire document (e.g., the summary).

Claims 1-3, 6-13, 27, 29, 56, 57, and 59 are directed to a genus of polypeptides, which comprise amino acid sequence differing from the amino acid sequence set forth as SEQ ID NO: 1, as the members of the genus are variants of the polypeptide of SEQ ID NO: 1, polypeptides comprising a mere fragment of SEQ ID NO: 1, derivatives of SEQ ID NO: 1, and fusion proteins comprising said variants, polypeptides comprising mere fragments, and derivatives. The claims are thus directed to a genus of polypeptides having highly variable structures and are not limited to a polypeptide comprising the amino acid sequence of SEQ ID NO: 1 from the amino acid at position 20 (methionine) through the amino acid at position 659 (tyrosine).

While the specification teaches a polypeptide comprising the amino acid sequence of SEQ ID NO: 1 from the amino acid at position 20 (methionine) through the amino acid at position 659 (tyrosine), the specification does not teach variants, including naturally occurring variants, of the polypeptide. Furthermore, the specification does not teach other polypeptides that comprise a mere fragment of the amino acid sequence of the polypeptide of SEQ ID NO: 1.

Notably, claims 1-3, 7-12, 27, 29, 56, and 57 are not limited to polypeptides having any one particular function; and although claims 6, 13, and 59 limit the members of the genus of polypeptides to polypeptides that have "migration stimulating factor activity", the functional activity or activities that constitute "migration stimulating factor activity" have not been disclosed. Moreover, the specification fails to teach an assay by which such a polypeptide having "migration stimulating factor activity" can be recognized or distinguished from other polypeptides.

Because the detailed structures of the variants of the polypeptide of SEQ ID NO; 1, including naturally occurring variants, and other polypeptides comprising a fragment of the sequence are not disclosed, and because an assay by which the claimed polypeptides can be recognized and isolated is not disclosed, the skilled artisan would

first have to perform an undue amount of additional experimentation to determine how the polypeptides can be made, isolated, purified, characterized, and/or recognized.

While the prior art teaches that the polypeptide of SEQ ID NO: 1 (i.e., MSF) is capable of stimulating the migration of fibroblasts that do not express the polypeptide into a collagen matrix, the specification does not teach that this is the functional activity that constitutes the "migration stimulating factor activity" of the polypeptides to which claims 6, 13, and 59 are directed. Notably, the specification teaches only that MSF is believed to be involved in the migration of cells, especially fibroblasts; see, e.g., page 41, lines 24-26. With regard to claims 1-3, 7-12, 27, 29, 56, and 57, unless the polypeptides to which the claims are directed share or retain the ability of MSF, as taught by the prior art, to stimulate the migration of fibroblasts that do not express the polypeptide into a collagen matrix, the skilled artisan would have to perform an undue amount of additional experimentation to determine how the polypeptides could otherwise be used. With further regard to claims 12, 56, and 57, which are directed to any polypeptide that can be produced by culturing the host cell of claim 8, it is aptly noted that the amount of guidance, direction, and exemplification provided by the instant disclosure is not reasonably commensurate in scope with the claims, since the vast majority of the polypeptides do not have functions that are shared by the polypeptide of SEQ ID NO: 1. Unless the prior art teaches the skilled artisan to use any given polypeptide produced by the host cell of claim 8, the skilled artisan would have to elaborate a use for the polypeptide, and this would require that an undue amount of additional experimentation be performed before its use.

The skilled artisan cannot reliably and accurately predict whether a variant of the polypeptide of SEQ ID NO: 1 or a polypeptide comprising a mere fragment of the amino acid sequence is capable of being used the same manner as the polypeptide of SEQ ID NO: 1. For example, Skolnick et al. (*Trends in Biotechnology* 2000; **18**: 34-39) discloses that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see, e.g., the abstract; and page 34, *Sequence-based approaches to function prediction*). Even in situations where there is

some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see, in particular, the abstract and Box 2). Thus, one skilled in the art would not accept an assertion, which is based only upon some observed similarity in amino acid sequences, that a variant of the polypeptide of SEQ ID NO: 1, or a polypeptide comprising a mere fragment of the amino acid sequence would be capable of being used the same manner as the polypeptide of SEQ ID NO: 1 (i.e., MSF). Accordingly, an undue amount of additional experimentation would first have to be performed before the claimed invention could be used as MSF is used, because before it could be used, the functional activities of the claimed protein would have to be determined empirically.

In addition to naturally occurring variants of the polypeptide of SEQ ID NO: 1, the claims are directed to engineered variants, but notably the specification fails to teach which amino acid residues of SEQ ID NO: 1 are critical to the function of the protein. Furthermore, the specification fails to teach by which other amino acids such critical residues can be replaced without loss of activity. The skilled artisan cannot reliably and accurately predict the effects of amino acid substitutions, deletions, or insertions in the amino acid sequence of a given polypeptide. Even a single nucleotide alteration in the amino acid sequence of SEQ ID NO: 14 can drastically alter both the structure and function of the variant. Burgess et al. (*Journal of Cell Biology* **111**: 2129-2138, 1990) exemplifies the sensitivity of proteins to alterations of even a single amino acid in a sequence. Burgess et al. teaches that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. As another example of this sensitivity to amino acid sequence variations, Lazar et al. (*Molecular and Cellular Biology*, 1988, **8**: 1247-1252) teaches that a replacement of aspartic acid at position 47 with alanine or asparagine in transforming growth factor alpha had no effect but that a replacement with serine or glutamic acid sharply reduced its biological activity. Thus, Lazar et al. teaches that even a single *conservative* type amino acid substitution may adversely affect the function of a protein. Therefore, again, an undue

amount of additional experimentation would first have to be performed before the claimed invention could be made and used, because it would first be necessary to empirically determine which amino acid residues of the polypeptide are critical to its function and by which other amino acids the critical residues could be replaced without loss of the function.

Claim 56 is drawn to a pharmaceutical composition comprising one of the polypeptides to which the claims are directed, including the polypeptide of SEQ ID NO: 1, whereas claim 57 is drawn to one of the polypeptide for use in medicine.

The specification teaches the invention provides or includes a number of therapeutic applications, including chemoprevention and chemotherapy; see, e.g., page 40, lines 20 and 21. The specification teaches the polypeptide can be administered to a site of cell migration or wound healing within a mammalian body, including a human; see, e.g., page 42, line 4, through page 4, line 19. Alternatively, the specification teaches that the polynucleotide encoding the polypeptide provides a means for controlling the expression of the polypeptide by gene therapy; see, e.g., page 44, lines 10 and 11.

However, it is again noted that the specification teaches only that MSF is believed to be involved in the migration of cells, especially fibroblasts; see, e.g., page 41, lines 24-26. The specification does not actually show that the activity or expression of the polypeptide, or the lack thereof, is causative of any particular disease or condition. Moreover, the specification does not provide any factual evidence to support the assertion that the invention can be used or provides a means for treating or preventing a disease (e.g., cancer) or disorder (e.g., wounds). Absent such factual evidence, the skilled artisan would not accept an assertion, for example, that administering the polypeptide to a mammal at the site of a wound would provide any therapeutic benefit to the mammal.

Although the prior art suggests the polypeptide of SEQ ID NO: 1 has a possible role in certain diseases and wound healing, regarding the possibility that the claimed invention might be therapeutically useful, it is aptly noted that the art of drug discovery for is highly unpredictable. With regard to anticancer drug discovery, for example, Gura

(*Science* 1997; **278**: 1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile (abstract). Gura teaches that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models, but that only 39 have actually been shown to be useful for chemotherapy (page 1041, first and second paragraphs). Moreover, because of the lack of predictability in the art, Gura discloses that often researchers merely succeed in developing a therapeutic agent that is useful for treating the animal or cell that has been used as a model, but which is ineffective in humans, indicating that the results acquired during pre-clinical studies are often non-correlative with the results acquired during clinical trials (page 1041, column 2). Because the skilled artisan cannot predict whether any given polypeptide or nucleic acid can be used as a therapeutic agent, absent exemplification of such use of the claimed invention, an undue amount of additional experimentation would have to be performed before it could be used.

Furthermore, regarding any possibility that the claimed invention provides a marker that might be diagnostically useful, Ward (*Developmental Oncology* 1985; **21**: 91-106), for example, teaches not all markers can be reliably used in primary diagnosis. Ward teaches that a number of tumor-associated markers are, in fact, diagnostically unreliable. Rather, Ward teaches some markers are more useful as guides in monitoring the efficacy of treatment modules for malignant disease. Because the skilled artisan cannot predict whether any given polypeptide or nucleic acid can be used as a diagnostic marker, absent exemplification of such use of the claimed invention, an undue amount of additional experimentation would have to be performed before it could be used.

In conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with *Ex parte Forman*, 230 USPQ 546 (BPAI 1986), the amount of guidance, direction, and exemplification disclosed by Applicant is not deemed sufficient to enable the skilled artisan to use the claimed invention without a need to perform an undue amount of additional experimentation.

21. Claim 8 is further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using an isolated host cell comprising a recombinant polynucleotide according to claim 1 or a replicable vector comprising said polynucleotide, does not reasonably provide enablement for making and using any such host cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 8 is drawn to a host cell comprising a recombinant polynucleotide according to claim 1 or a replicable vector comprising said polynucleotide. The claim is broadly interpreted to encompass host cells, which are not isolated and are comprised within an organism. Thus, the claims encompass host cells that have been transfected with a polynucleotide according to claim 1 or a vector according to claim 7, which cells are comprised within an animal, including nonhuman or human animals, treated using gene therapy.

Support for this broad interpretation of the claim is found throughout the specification; see, e.g., page 42, lines 6-8; and page 44, lines 10 and 11.

The teachings of the specification cannot be extrapolated to the enablement of the claimed invention because the amount of guidance, direction, and exemplification set forth therein would not be sufficient to enable the skilled artisan to make and use the claimed invention without the need to perform additional, and an undue amount of experimentation. Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The specification does not provide a sufficient amount of guidance, direction, or exemplification to enable the skilled artisan to make or use host cells that are comprised

within a non-human transgenic animal. In the art of producing transgenic animals, the phenotype of the resultant transgenic animal is not always predictable; nor is the transgenic embryo always viable. Houdebine (*Journal of Biotechnology* 1994, 34: 269-287) teaches the vectors to be used for directing the expression of transgenes in any given tissue, or in all tissues, must contain the appropriate regulatory regions; see entire document (e.g., paragraph bridging pages 272 and 273). Houdebine teaches expression is heavily dependent on the site of integration in the host genome and the site of integration is presently unpredictable (page 27, column 1). Therefore, it is concluded that one of skill in the art would need to perform an undue amount of experimentation in order to make and use the claimed host cell comprised within a transgenic animal.

In addition, the specification does not teach provide a sufficient amount of guidance, direction, and exemplification to enable the skilled artisan to have a reasonable expectation of successfully producing the claimed host cells within a living organism by gene transfer, or *gene therapy*. The art of gene therapy, i.e., the *in vivo* delivery genetic information to targeted cells within a body using naked DNA or viral vectors or by reintroducing *ex vivo* modified host cells into the body, is still in its infancy. Moreover, the art is highly unpredictable and its successful application has been hindered by numerous limitations, which the specification does not remedy and would preclude the skilled artisan from having a reasonable expectation of successfully making and using the claimed invention without need of performing an undue amount of experimentation.

For example, the teachings of the specification have not overcome the problems with *in vivo* delivery and expression. Verma et al. (*Nature* 1997, **389**: 239-242) teaches that the Achilles heel of gene therapy is gene delivery (page 239, column 3). Verma et al. states that the ongoing problem is the inability to deliver genes efficiently and to obtain sustained expression; see entire document (e.g., page 239, column 3). Similarly, Amalfitano et al. (*Current Gene Therapy* 2002, **2**: 111-133) teaches that non-viral mediated transfer of DNA generally suffers from low transduction efficiencies; see entire document (e.g., page 111, column 2). In addition, Amalfitano et al. discusses numerous

limitations that have been encountered in using retroviral vectors to deliver DNA into a subject and teaches the use of adenoviral vectors can be ineffective because of the induction of strong immune responses in the host to the viral vectors and direct acute and chronic toxicity caused by the vector itself; see entire document (e.g., abstract).

It is noted that Amalfitano et al. teaches that a despite general lack of success, the first conclusive evidence that gene therapy can show efficacy in humans was achieved in human X-linked SCID subjects *via* retrovirus transduction (page 111, column 2). However, since the publication, The Department of Health and Human Services has released a memorandum dated January 14, 2003, a copy of which is attached to this Office action, that urges all such investigations to be discontinued until new data are available, the possible etiology and risks of adverse events associated are considered, and recommendations emerge. Despite the initial promise of the trial studying gene transfer as a possible treatment for the disease, investigators have found that retroviral-mediated insertion of the transgene has caused the subjects to develop cancer. The results of the trial underscore the high degree of unpredictability associated with the art and the fact that the skilled artisan could not make or use the claimed invention with a reasonable expectation of success without need to perform additional and an undue amount of experimentation.

The state of the art, as a whole, is well defined by Pandha et al. (*Current Opinion in Investigational Drugs* 2000; **1** (1): 122-134). Pandha et al. teaches:

> Despite the rapid technological advances that continue to sustain the field of cancer gene therapy, few individual patients have benefited from the revolution so far. The plethora of clinical trials described confirms that each malignancy will have its own ideal strategy based on the associated molecular defects, and there has been rapid progress from this viewpoint. At the same time, there has been a renewed appreciation for the limitations to gene therapy, which include low efficiency of gene transfer, poor specificity of response and methods to accurately evaluate responses, and lack of truly tumor-specific targets at which to aim. As with all new therapies, we are climbing a steep learning curve in terms of encountering treatment-related toxicities, as well as profound ethical and regulatory issues (abstract).

In view of the preponderance of evidence establishing the state of the art, now and at the time the application was filed, and the level of unpredictability associated therewith, in the absence of a disclosure of an amount of guidance, direction, and

exemplification that is reasonably commensurate in scope with the claims, it appears that skilled artisan could not make and use the claimed invention with a reasonable expectation of success without having the need to perform an undue amount of experimentation.

This issue can be remedied by amending claim 8 to recite "isolated" before "host cell".

22. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

23. Claims 6, 13, and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6, 13, and 59 are indefinite because the claims recite a limitation that the polypeptide has "migration stimulating factor activity". The specification does not teach what functional activity or activities constitutes "migration stimulating factor activity". Moreover, the specification does not teach an assay by which it can be determined whether a given polypeptide has "migration stimulating factor activity". Accordingly, the metes and bounds of the subject matter that Applicant regards as the invention cannot be determined.

Claim Rejections - 35 USC § 102

24. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

25. Claims 10-13, 27, 29, 56, 57, and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Grey et al. (*Proc. Natl. Acad. Sci. USA*. 1989 Apr; **86**: 2438-2442)

(of record), as evidenced by Schor et al. (*Cancer Res.* 2003 Dec; **63** (24): 8827-8836).

Claims 10-13, 27, 29, 56, 57, and 59 are drawn to a polypeptide, or a composition thereof, comprising the amino acid sequence set forth as SEQ ID NO: 1.

Grey et al. teaches a purified polypeptide having an estimated molecular mass of 70 KDa; see entire document (e.g., the abstract). Grey et al. teaches the polypeptide is normally produced by human skin fibroblasts of fetal origin, but not of adult origin (abstract). Grey et al. designates this purified polypeptide, "migration stimulating factor" (MSF) (abstract).

As evidenced by Schor et al., the polypeptide disclosed by Grey et al. is the same as the polypeptide of SEQ ID NO: 1, which sequence comprises SEQ ID NO: 3; see entire document (e.g., page 8827, column 2; page 8829, Figure 2. For example, Shor et al. teaches the polypeptide disclosed by Grey et al. comprises an amino acid sequence that terminates with a unique 10 amino acid sequence that is not present in any previously identified isoform of fibronectin; this 10 amino acid sequence is identical to the carboxy-terminal 10 amino acids of SEQ ID NO: 1. In addition, Shor et al. teaches that the purified polypeptide produced by fetal fibroblasts is functionally and structurally indistinguishable from recombinant polypeptide; see, e.g., page 8830, column 2, through page 8831, column 1; and page 8832, column 1. Therefore, although Grey et al. does not teach that the purified polypeptide comprises the amino acid sequence set forth as SEQ ID NO: 1, absent a showing of any difference, the polypeptide disclosed by Grey et al. is deemed the same as the polypeptide of SEQ ID NO: 1.

Grey et al. does not expressly teach that MFP has "migration stimulating factor activity", but it is noted that Grey et al. teaches the polypeptide stimulates the migration of fibroblasts that do not express the polypeptide into a collagen matrix; see, e.g., page 2439, column 1; and page 2441, Figure 1. Nevertheless, because the specification does not define what functional activity or activities constitute "migration stimulating factor activity", absent a showing of any difference, MFP is deemed the same as a polypeptide having such activity.

Notably, the Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the claimed polypeptide. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed polypeptide is different than that taught by the prior art.

26. Claims 1-3, 6-13, 27, 56, 57, and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 94/16085 A2 (of record).

The claims are directed to a recombinant polynucleotide encoding a polypeptide comprising a variant, fragment, or derivative of the amino acid sequence set forth as SEQ ID NO: 1.

WO 94/16085 A2 (Irani et al.) teaches a polypeptide that comprising a variant of SEQ ID NO: 1; see entire document (e.g., pages 37-48, SEQ ID NO: 1). Furthermore, the polypeptide disclosed by Irani et al. comprises a fragment of SEQ ID NO: 1 and, absent a showing of any difference, the polypeptide is deemed to comprise a derivative of SEQ ID NO: 1. Irani et al. teaches a recombinant polynucleotide encoding the polypeptide, a replicable vector comprising the polynucleotide, a host cell comprising the vector, and a method for producing the polypeptide comprising culturing the host cell and isolating the polypeptide; see, e.g., page 3, line 22, through page 4, line 8; and page 10, line 18, through page 15, line 12.

27. Claims 12, 56, 57, and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Bristow (*Trends Biotechnol.* 1993 Jul; **11** (7): 301-305), as evidenced by Benoliel et al. (*J. Cell Sci.* 1997 Sep; **110** (Pt 17): 2089-2097).

Claim 12 is a product-by-process claim, which is drawn to a polypeptide. Claims 12, 56, 57, and 59 read on any polypeptide that could be produced by a process comprising culturing a host cell according to claim 8. Thus, the claims are not limited to a polypeptide that comprises SEQ ID NO: 1; nor are the claims limited to a polypeptide comprising a variant, fragment, or derivative of SEQ ID NO: 1.

Bristow teaches a polypeptide, namely insulin, which can be produced using a host cell comprising an expression vector encoding the polypeptide; see entire document (e.g., the abstract).

Bristow does not expressly teach that insulin has "migration stimulating factor activity", but as evidenced by Benoliel et al., insulin stimulates haptotactic migration of keratinocytes; see entire document (e.g., the abstract). Nevertheless, the specification does not define what functional activity or activities constitute "migration stimulating factor activity", absent a showing of any difference, insulin is deemed the same as a polypeptide having such activity.

Again, the Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the claimed polypeptide. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed polypeptide is different than that taught by the prior art.

Claim Rejections - 35 USC § 103

28. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

29. Claims 1-3 and 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grey et al. (*Proc. Natl. Acad. Sci. USA.* 1989 Apr; **86**: 2438-2442) (of record), as evidenced by Schor et al. (*Cancer Res.* 2003 Dec; **63** (24): 8827-8836), in view of Bendig (*Genet Eng.* 1988; (7): 91-127).

Claims 1-3 and 6-9 are drawn to a recombinant polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 1, a replicable vector

comprising the recombinant polynucleotide, a host cell comprising the recombinant polynucleotide or the vector, and a method for making the polypeptide encoded by the recombinant polynucleotide by a process comprising culturing the host cell.

Grey et al. teaches that which is set forth above in the rejection of claims 10-13, 27, 29, 56, 57, and 59 under 35 USC § 102(b).

However, Grey et al. does not expressly teach a recombinant polynucleotide encoding MSF; nor does Grey et al. expressly teach culturing a host cell comprising a replicable vector comprising a polynucleotide encoding MSF to produce the polypeptide.

Bendig et al. reviews methods for producing foreign proteins in mammalian host cells by recombinant DNA technology; see entire document (e.g., the abstract). Bendig teaches that a DNA molecule can be produced or isolated, which encoded a given protein; see, e.g., the abstract. Bendig teaches that a replicable vector comprising the polynucleotide sequence of the DNA molecule encoding the protein can be introduced into a suitable host cell; see, e.g., the abstract. Bendig teaches the host cell comprising the vector can be cultured to produce the protein; see, e.g., the abstract. Bendig teaches the polypeptide can be isolated; see, e.g., the abstract.

It would have been *prima facie* obvious to one ordinarily skilled in the art at the time of the invention to produce MSF by culturing a host cell comprising a vector comprising a polynucleotide sequence encoding the polypeptide by recombinant DNA technology in accordance with the teachings reviewed by Bendig et al. One ordinarily skilled in the art at the time of the invention would have been motivated to do so to produce the polypeptide.

Conclusion

30. Claims 4 and 5 are allowed. No other claims are allowed.

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
November 29, 2004